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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/591,451

06/04/2007

Ernestine Lee

08940.0038

9377

22852

7590

12/02/2009

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EXAMINER

LEAVITT, MARIA GOMEZ

ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

12/02/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/591,451	<b>Applicant(s)</b> LEE ET AL.	
	<b>Examiner</b> MARIA LEAVITT	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 03 September 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1, 5, 6, 8, 13, 16-18, 23, 30-32, 34-36, 41, 44, 49, 52, 53, 55, 64, 70, 74, 76, 78, 80 is/are pending in the application.
- 4a) Of the above claim(s) 35, 36, 44, 49, 52, 53, 55, 64, 70, 74, 76 and 78 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34 and 41 and 80 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>01-15-2008</u> .  | 6) <input type="checkbox"/> Other: _____                          |

Art Unit: 1633

***Detailed Action***

Claims 1, 5, 6, 8, 13, 16-18, 23, 30-32, 34-36, 41, 44, 49, 52, 53, 55, 64, 70, 74, 76, 78 and 80 are pending. Applicants' election with traverse of Group II, drawn to a polypeptide, i.e., claims 8, 13, 16, 17, 31 and 41 in Applicants' response filed on 09-03-2009 is acknowledged. Additionally, Applicants' election with traverse of SEQ ID NO: 215 is acknowledged.

***Response to Applicants' arguments***

At page 2 of Applicants' remarks filed on 09-03-2009, Applicants' traversal is that there is no undue burden to do a search of non elected invention, particularly, examination of Groups I to XI. The above argument has been fully considered but deemed unpersuasive.

Applicant's argument of search burden is not found persuasive, because instant application is a national stage filing under 35 U.S.C. 371 and according to MPEP 1893.03(d), whether or not a serious burden is required is not a proper basis of traversal in a national stage application. In the instant case, the "special technical feature" is novel polynucleotides or fragments thereof, related polypeptides related nucleic acid and polypeptide compositions corresponding to novel human cDNA clones useful in treating proliferative disorders. The prior art has taught human cDNA clones including the polynucleotide sequences of AAA39052 to AAA39088 which encode the human secreted proteins given in AAB08891 to AAB08984 which are useful for treating disorders of the immune system, hyperproliferative disorders, infectious disease and others. Thus, instant technical feature does not contribute over prior art.

However, in reviewing the requirements for election restriction mailed on 06-03-2009, the examiner is withdrawing the restriction requirements between Groups I, i.e., 1, 5, 6, 18, 23,

Art Unit: 1633

30, 32, 34 and 80) and II as both groups encompass an isolated nucleic acid molecule encoding the corresponding amino acid peptide.

Therefore, claims 35, 36, 44, 49, 52, 53, 55, 64, 70, 74, 76 and 78 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected invention, there being no allowable generic or linking claim.

The requirement is deemed proper and is therefore made FINAL.

Therefore, claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 are currently under examination on the merits to which the following grounds of rejection are applicable. Note that generic claims 1 and 8 are examined to the extent that they read on the elected invention: a nucleic acid molecule comprising a first polynucleotide or a biologically active fragment thereof encoding a corresponding polypeptide comprising SEQ ID NO: 215 and a polypeptide comprising a first amino acid sequence comprising the amino acid sequence of sequence 215 or a biologically active fragment thereof.

#### ***Information Disclosure Statement***

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

#### ***35 USC 101-non-statutory subject matter***

35 U.S.C. §101 states:

Art Unit: 1633

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 are rejected under 35 USC §101 because the claimed invention is directed to non-statutory subject matter.

Claim 1 recites “a nucleic acid molecule”. Likewise, claim 8 recites the phrase “a polypeptide comprising a first amino acid sequence”. As written, claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 do not sufficiently distinguish over cells on their own right that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught at paragraph [0018] of the PGPUB 20070258949. See MPEP 2105.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 1 is indefinite in the recitation of “a biologically active fragment or any of (a) –(c)” . Likewise, claim 8 is indefinite in the recitation of “a biologically active

Art Unit: 1633

fragment or any of (a) or (b)”, as it is unclear as to what “a biologically active” or activities are intended as being encompassed by the noted phrase. Proteins are known in the prior art to have numerous activities, both specific and general. For example, all proteins of a sufficient length are known to have the activity of eliciting an antibody or immune response. It is suggested that applicant clarify the intended meaning of the noted phrase.

Claims 5, 6, 18, 23, 30, 32, 34 and 80 are indefinite insofar as they depend from claim 1 and claims 13, 16, 17, 31 and 41 are indefinite as they depend from claim 8.

***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim(s) 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

According to MPEP 2163.II.A.1, in evaluating a claimed invention for adequate written description, the examiner should determine what the claim as a whole covers. “Claim construction is an essential part of the examination process. Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the

Art Unit: 1633

written description. See, e.g., *In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997).”

Claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 can be broadly but reasonably interpreted as encompassing a genus of nucleic acid molecules that are variants/fragments of the nucleic acid encoding the polypeptide comprising the amino acid sequence of SEQ ID NO: 215, a 79-residue amino acid sequence. Moreover, the claims are broadly drawn to any biologically active fragment of the peptide of SEQ ID NO: 215 comprising any fragments or portion of SEQ ID NO: 215, wherein the genus of nucleic acid sequences and peptides are not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made. It is noted that the claims encompass “biologically active fragments” that have beneficial or adverse effects on any sort of living matter. Thus, the genus of nucleic acid molecules/ peptides encompasses any length of nucleic acid molecule encoding for the peptide of SEQ ID NO: 215 and any peptide that can be fragments with or without the claimed biological activity.

The specification at paragraph [0048] provides a definition of the phrase “biologically active” entity as “is one having structural, regulatory, or biochemical functions of a naturally occurring molecule or any function related to or associated with a metabolic or physiological process” and at paragraph [0079] discloses “the invention provides an isolated polypeptide comprising an amino acid sequence, wherein the amino acid sequence is chosen from the Sequence Listing or the tables, or a biologically active fragment thereof, or is encoded by a polynucleotide sequence chosen from Sequence Listing or the tables, or a biologically active fragment thereof, such as, for example, any one of SEQ ID NOS:188-374”. Moreover, the

Art Unit: 1633

specification discloses prophetically in Examples 1-13, various assays to test for the biological activity of the claimed fragments of nucleic acid molecules and/or peptides.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention (January 5, 2001 Fed. Reg., Vol. 66, No. 4, pp. 1099-11). The court and the Board have repeatedly held (*Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. It is not sufficient to define DNA solely by its principal biological property, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid or protein,



Art Unit: 1633

so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. Also, where a claim purports to cover all nucleic acids that encode a specific protein and the specification discloses but a single DNA known to do so, the situation is analogous to a single means claim and does not meet the enablement requirement under para. 1 of §112. The court has also held that a claimed nucleic acid could meet the written description and enablement requirements if the nucleic acid were defined by a disclosed process found, after-the-fact, to produce the nucleic acid, and claimed as a product-by-process. However, in the instant case, the nucleic acids are not claimed as a product-by-process, nor does the specification disclose any process known to yield a claimed nucleic acid.

Overall, what these statements indicate is that the Applicant must provide adequate description of such core structure and function related to that core structure such that the Artisan could determine the desired effect. Hence, the analysis below demonstrates that Applicant has not determined the core structure for full scope of the claimed genera.

In the instant case, applicants only disclose the peptide of SEQ ID NO: 215 and contemplate various functionalities for the claimed nucleic acid molecules and/or peptides in diagnostic, prophylactic, and therapeutic applications for a variety of diseases including killing human tumor cells, e.g., solid or leukemic human tumor treatment of prostatic or pancreatic tumors, breast tumor cells, colon tumor cells, lung tumor cells, bladder tumor cells, stomach tumor cells, kidney tumor cells, testicular tumor cells, endocrine tumor cells, or skin tumor cells

Art Unit: 1633

[0023]. However, the specification fails to provide any specific guidance about which portion of the sequence could be modified e.g., added/ or deleted and still retain full or even partial activity for the claimed treatment of tumors. Applicants are claiming other forms of nucleic acid molecules and/or peptides variants of the peptide of SEQ ID NO: 215, by function only, without a correlation between structure and function. Applicants provide no disclosure of what structural feature(s) of the instantly disclosed peptide of SEQ ID NO: 215 and corresponding nucleic acid are responsible for the diagnostic, prophylactic or treatment of any specific disorder. Given the diversity of the claimed variants and/or fragments of SEQ ID NO: 215 with any biological activity, it is incumbent upon the specification to disclose means for identifying such SEQ ID NO: 215 variants commensurate in scope with coverage sought by the claims.

The skilled artisan understands that one nucleotide change in a DNA molecule or one amino acid change in the polypeptide encoded by the DNA molecule could result in the loss of its biological activity as demonstrated in the generation of sickle-cell anemia wherein on specific amino acid mutation gave rise to the inherited disease (Biochemistry, John Wiley and Sons, 1990, p. 126-129). Furthermore, it is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Hence, even single-nucleotide polymorphism without affecting the amino acid sequence can affect folding of the protein and thus alter its function (Kimchi-Sarfaty et al., 2007, Science, pp. 525-528; p. 527, col. 3, last paragraph). Rudinger (in

Art Unit: 1633

Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976) discloses that even for peptide hormones, which are much smaller than the instant peptide of SEQ ID NO:215 of 79 amino acids, one cannot predict variant amino acid sequences for a biologically active polypeptide. Rather one must engage in "case to case painstaking experimental study" to determine active variants (see page 7). Thus the ability to determine *a priori* whether a mutation in a region critical to the claimed structure/function of the nucleic acid molecule/ peptide relationship, particularly, various sites or regions directly involved in the activity of the molecule is not predictable.

Though the specification teaches that the peptide of SEQ ID NO: 215 can selectively be used for diagnostic, prophylactic, and therapeutic treatment for a variety of diseases, this may not be sufficient, as the ordinary artisan would immediately recognize that there is not disclosure of A) regions of the encoded peptide structure which may be modified without affecting its activity; (B) the general tolerance of SEQ ID NO: 215 peptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in SEQ ID NO: 215 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Thus, it is not possible from reading the examples to envision what types of mutations have been introduced, or how many mutations have been introduced in each modified nucleic acid molecule and corresponding peptide of SEQ ID No. 215 to result in selectively diagnostic, prophylactic, and therapeutic treatment for a variety of diseases.

Neither applicants nor the prior art disclose other peptides that comprise a functional SEQ ID NO: 215 peptide other than the full-length of SEQ ID No. 215 and the corresponding

Art Unit: 1633

nucleic acid sequence. Applicants provide no disclosure of what structural feature(s) of the instantly disclosed peptide of SEQ ID No. 215 are responsible for the claimed biological activities.

Thus, the recited structural relationship is arbitrary since neither the specification nor the prior art discloses any definitive relationship between peptide function and % identity or homology at the amino acid level; and the specification does not describe a single species of nucleic acid that encodes a functional peptide that is not either 100% identical to SEQ ID NO: 215 or that encodes a peptide that is not 100% identical to SEQ ID NO: 215.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus, and thus, that the applicant was not in possession of the recited genus. The claimed subject matter is not supported by an adequate written description because a representative number of species has not been described.

Claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 215 and corresponding nucleic acid sequence, does not reasonably provide enablement the claimed genus of polynucleotides and/or/polypeptide variants/fragments as broadly encompassed by the claims.

The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to use the invention commensurate in scope with this claim. Factors to be considered in determining whether a disclosure meets the enablement requirement

Art Unit: 1633

of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

According to MPEP 2164.04, “[b]efore any analysis of enablement can occur, it is necessary for the examiner to construe the claims...and explicitly set forth the scope of the claim when writing an Office action.” Also, MPEP 2164.08 states, “[w]hen analyzing the enabled scope of a claim, the teachings of the specification must not be ignored because claims are to be given their broadest reasonable interpretation that is consistent with the specification.”

Claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 can be broadly but reasonably interpreted as encompassing a genus of nucleic acid molecules that are variants/fragments of the nucleic acid molecule encoding the polypeptide comprising the amino acid sequence of SEQ ID NO: 215, a 79-residue amino acid sequence. Moreover, the claims are broadly drawn to any biologically active fragment of the peptide of SEQ ID NO: 215 comprising any fragments or portion of SEQ ID NO: 215, wherein the genus of nucleic acid sequences and peptides are not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made. Note, at paragraph [0048], the specification defines a “biologically active” entity as “one having structural, regulatory, or biochemical functions of a naturally occurring molecule or any function related to or associated with a metabolic or physiological process”. Accordingly, the “biological active fragments” can be reasonably

Art Unit: 1633

interpreted as encompassing a genus of biological activities such as stimulating an immune response, participating in signal transduction, fatty acid synthesis and others. It is noted that the claims encompass “biologically active fragments” that have beneficial or adverse effects on any sort of living matter.

In the instant case, applicants only disclose a single peptide of SEQ ID NO: 215 from human tissue e.g., testis, encoded by the cDNA clone CLN00156143 (see, Specification paragraph [0058] and Table 4, FP ID HG1014930 corresponding to SEQ ID NO: 215). Neither applicants nor the prior art disclose other peptides of SEQ ID NO: 215 from another source that is predicted as a non secreted peptide (see Table 2 for predicting the likelihood that the FP ID HG1014930 is secreted). In fact, FP ID HG1014930 as shown in Table 5 only displays no more 53% homology , (ID Mat (HL)) to polypeptide sequences from the NCBI database. Applicants are claiming other forms of peptides variants of the human peptide of SEQ ID NO: 215, by function only, without a correlation between structure and function. Applicants provide no disclosure of what structural feature(s) of the instantly disclosed SEQ ID NO: 215 are responsible for any of the claimed activities relatives to other human disclosed polypeptides. Given the diversity of the claimed nucleic acid molecules and corresponding amino acid sequences that are variants of the peptide of SEQ ID NO: 215, it is incumbent upon the specification to disclose means for identifying such variants of the peptide of SEQ ID NO: 215 commensurate in scope with coverage sought by the claims. The diversity of the peptide of SEQ ID NO: 215 and DNA sequences claimed, along with the lack of disclosure regarding other human peptides of SEQ ID NO: 215 and variants, would require the skilled artisan to conclude

Art Unit: 1633

that the single predicted non secreted human peptide of SEQ ID NO: 215 presented by the applicants is not sufficient to describe the claimed genus.

The specification does not provide any information on what amino acid residues are necessary and sufficient for the disclosed biological active properties, such as treatment of cancer or relative sources of peptides of SEQ ID NO: 215 other than human tissue. The specification also provides no teachings on what amino acid sequence modifications, e.g. insertions, deletions and substitutions, would be permissible in a variant polypeptide that would improve or at least would not interfere with the biological activity or structural features necessary for the biological activity and stability of the peptide. Since there were no other examples of a functional peptides of SEQ ID NO: 215 known that have structural homology with SEQ ID NO: 215, it is not possible to even guess at the amino acid residues which are critical to its structure or function based on sequence conservation. The comparison of SEQ ID NO: 215 to other human peptide sequences is no help because of the lack of sequence conservation (i.e. less than 53%, Table 5). Furthermore, it is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976) discloses that even for peptide hormones, which are much smaller than the instant peptide of SEQ ID NO: 215, one cannot predict variant amino acid sequences for a biologically active polypeptide. Rather one must engage in "case to case painstaking experimental study" to

Art Unit: 1633

determine active variants (see page 7). Consequently, excessive trial and error experimentation would have been required to identify the necessary derivatives of SEQ ID NO: 215 with an activity of SEQ ID NO: 215 since the amino acid sequence of such polypeptides could not be predicted - even if the activities were known.

As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required to make and use all methods as broadly encompassed by the claims, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is



Art Unit: 1633

unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102(b)***

To the extent that claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 broadly read on an isolated nucleic acid molecule and corresponding polypeptides comprising a variant/fragment of the amino acid sequence of SEQ ID NO: 215, the following rejection applies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 are rejected under 35 USC. 102(b) as being anticipated by Rosen et al., (WO 00/55200 International Publication Date 21 September 2000; See SCORE Search Results Details for Application 10591451 and Search Result 20091110\_135148\_us-10-591-451-215.rag. Result2).

Rosen et al., teaches isolated human secretory proteins and nucleic acids encoding them useful for diagnosing and treating disorders related to the proteins such as cancer, Alzheimer's disease and Parkinson (page 2, lines 9-15). Specifically, Rosen discloses a 92-residue nucleic acid molecule having an amino acid homology of 43.4% to the amino acid sequence of SEQ ID NO: 215, a 79-residue amino acid sequence of the invention (See, Search Result 20091110\_135148\_us-10-591-451-215.rag. Result 2; page 93) (**Current claims 1, 8 and 23**). Absent evidence to the contrary, the nucleotide sequence of ID No. 1 of Rosen comprises regions

Art Unit: 1633

of full identity to SEQ ID NO: 215, including at least six contiguous amino acid residues (See SCORE Search Result 2, sequence alignment) (**Current claim 17**) . Additionally, Rosen teaches polynucleotides encoding for a “secreted” protein and mature forms of a protein (page 3, lines 1-7; page 6, line 25-30), fusion proteins (page 99, lines 5-15; page 111, lines 6-9; page 121, line 25-26; page 122, lines 11-25) (**Current claims 5, 6, 13, 16, 41 and 80**), vectors including a nucleic acid sequence of interest linked to a promoter (page 113, line 25-26; page 115, line 30) (**Current claim 18**), host cells (page 118, line 9-12) (**Current claim 34**) and pharmaceutical compositions (**Current claim 30-32**). Thus, the 92-residue amino acid sequence of Rosen et al., being 43.4% identical to the amino acid sequence of SEQ ID NO: 215 has all the properties cited in the invention and anticipate the instant invention.

### **Conclusion**

Claims 1, 5, 6, 8, 13, 16, 17, 18, 23, 30-32, 34, 41 and 80 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Art Unit: 1633

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/Maria Leavitt/

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